

AMENDMENT

In the Specification:

Please delete paragraph 29 on page 3 and renumber the paragraphs consecutively.

Please amend paragraph 110 on pages 31 and 32 as follows:

[110] This modeling enabled the investigation of the effect of potential separation between QD and DABCYL on the emission properties of the MB. Figure 14 shows models of the hybrid MB at two an arbitrary orientation orientations (~~close (Figure 14A)~~ and distant (Figure 14 14B) separation between QD and DABCYL). The models in this figure include idealized linear representations for linkers of the QD and DABCYL with correct local geometries in the absence of non-bonded contacts. It should be noted that the MB is capable of spanning a large conformational space, mediated by the multiple rotameric states of the aliphatic thiol linker of the QD and the linker of DABCYL and by typical DNA flexibility. In essence the only space excluded from occupation is the space that would produce atomic van der Waals clashes. In these figures, the orientation of the MB depicts the formation of Watson-Crick base pairs for the stem and a coil for the loop. A ribbon is overlaid on the DNA backbone. ~~Figure 14A shows~~ QD and DABCYL in close proximity is not shown. The distance from the center of the QD to the N=N bond of DABCYL (taken as the centre of DABCYL) is measured as about 3.3 nm. Figure 14 14B shows this distance to be about 5.0 nm. Since the separation between the center of QD and the N=N bond of DABCYL is between about 2 to about 10 nm, it satisfies the resonance energy transfer conditions. Under these circumstances, FRET efficiency for close proximity orientation and distant proximity orientation shown in Figure 14 14A and 14B are calculated as about 54% and about 9%, respectively. The Förster radius (where transfer efficiency is 50%) is calculated as about 3.4 nm for modified QD and DABCYL in the MB. See Kagan C.R., et al. (1996) Phys. Rev. B 54:8633; Vogelstein, B. and Kinzler, K.W. PNAS (1999) 96:9236-9241; Fang, X., et al. (2000) Anal.Chem. 72:3280-3285; and Tsuji, A., et al. (2000) Bioophys. J. 78:3260-3274, which are herein incorporated by reference. During this calculation the distance from the centre of QD to the N=N bond of DABCYL is used as practiced by others. See Medintz, I., et al. (2003) Nature Materials 2:630–638, which is herein incorporated by reference. The quantum yield of the modified QD is estimated as 6.8% by comparison with

fluorescein whose quantum yield is 0.92 in 0.1N NaOH. See Ratilainen, T., et al. (1998) Biochemistry 37:12331-12342, which is herein incorporated by reference. Since the separation between the center of the QD and DABCYL is less than about 10 nm, the energy emitted by QD can be quenched by DABCYL via FRET. It should be noted that potential variation in FRET efficiency due to dynamic spatial organization of the probe exists. Since the torsion angles of several chemical bonds attaching to both QD and DABCYL can assume several values spanning 360°, there are many possible spatial distributions for QD modified MBs. Especially inside a buffer solution, spatial distribution varies dynamically. These two models should be considered as snapshots of a conformationally dynamic macromolecule. This could change the separation distance between QD and DABCYL. However, as modeled this distance is less than about 10 nm which allows fluorescence quenching by FRET. For simplicity, both the core (CdSe) and the cap (ZnS) of QD are shown as a perfect sphere.

In the Drawings:

Please replace Sheets 8 and 9 with the replacement Sheets attached hereto.